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NATURAL SELECTIVE COOLING OF THE HUMAN BRAIN: EVIDENCE OF ITS OCCURRENCE AND MAGNITUDE

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SUMMARY

1. The technique of perceptual rating of thermal stimuli was used, in eight human subjects immersed in warm water, in order to appreciate whether they were hypo-, normo- or hyperthermic. Oesophageal, tympanic and forehead skin temperatures were recorded, as also was the temperature of the skin above the angularis oculi vein. Once the subjects gave clearly hyperthermic ratings, one arm was exposed to a 6 m/s wind. After 5–10 min the arm was re-immersed and the face was fanned.

2. Fanning of the arm resulted in lowering of body core temperature. However ratings of thermal stimuli remained hyperthermic.

3. Face fanning decreased forehead skin, angularis oculi vein and tympanic temperatures. Hyperthermic ratings were replaced by normothermic ratings, although oesophageal temperature continued to rise.

4. The upper limit of oesophageal temperature for normothermic ratings was $37{\cdot}06 \pm 0{\cdot}09$ °C during the control period without fanning. This temperature rose to $37{\cdot}91 \pm 0{\cdot}09$ °C during facial ventilation.

5. These results suggest a selective cerebral cooling due to venous blood returning from facial skin via the ophthalmic vein to the cavernous sinus, where a cooling of arterial blood ascending to the brain can take place.

INTRODUCTION

Metabolic heat production in the brain of a homeotherm is high relative to that of other tissues (Hales, 1973), while cerebral tissue is particularly prone to damage by hyperthermia (Burger & Fuhrman, 1964; Carithers & Seagrave, 1976). The continuous removal of heat from the brain by the circulating blood normally eliminates the risk of overheating. When general core temperature rises, however, the brain temperature also rises. Since the limit to the tolerable rise in core temperature appears to be that of the brain, any means of locally cooling the brain would increase heat tolerance.

Such brain cooling is known to occur in panting mammals which possess a carotid rete (Baker & Hayward, 1968; Baker, 1972; Taylor & Lyman, 1972; Kilgore, Bernstein & Schmidt-Nielsen, 1973; Baker & Chapman, 1977); the arterial blood is

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cooled immediately before it enters the brain by close contact with the cool venous blood returning from the nasal evaporative surfaces and other peripheral tissues of the head. Even in those panting mammals which lack a carotid rete, some brain cooling occurs (Caputa, Kadziela & Narebski, 1976).

Since the human does not possess a carotid rete and does not pant, it has been assumed that no such local cooling of brain tissue can occur. Cooling of the head skin, however, produces a significant improvement in the performance of heat stressed humans (Williams & Shitzer, 1974). This was attributed to a reduction in total body heat load but later McCaffrey, Geis, Chung & Wurster (1975*a*) suggested that the improved performance could be due, in part at least, to a local counter current heat exchange between cool blood in the jugular vein draining from the head skin and the blood ascending to the brain in the carotid artery. This hypothesis was based on the observation that total head cooling or more localized head skin cooling during hyperthermia was followed by a greater decrease in tympanic membrane temperature than in oesophageal temperature (McCaffrey *et al.* 1975*b*). Unfortunately, the relation between hypothalamic and tympanic temperature is unknown in the human and remains indeterminable. Cooling of the carotid arterial blood by local heat transfer to the jugular venous blood would seem unlikely since the major part of the jugular blood derives from the brain and is therefore warmer than the arterial blood passing to the brain.

The question whether, in any circumstance, there is selective cooling of the human brain remains unresolved, but Caputa, Perrin & Cabanac (1978) have shown that during hyperthermia in the human, facial venous blood flows strongly to the cavernous sinus through the angularis oculi and ophthalmic veins. Local heat exchange between the arterial blood passing to the brain, and the cooled venous blood returning from the facial skin is then possible.

Since human brain temperature cannot be measured directly, it is necessary to attempt a deduction of what is happening to the brain temperature during facial cooling, and this paper concerns such an attempt.

Clamping hypothalamic temperature in animals results in proportional, but opposite, shifts of deep trunk temperature, which equilibrate at the new open loop steady state (Hammel, Jackson, Stolwijk, Hardy & Strømme, 1963; Von Euler, 1964; Jessen & Clough, 1973). In this steady state, the animals do not present any thermoregulatory reaction and thus may be recognized as normothermic, although trunk and brain temperatures are significantly shifted in opposite directions. This observation indicates that if brain temperature is reduced to below general core temperature by local cooling of its arterial blood supply, there would be no thermoregulatory responses to a condition of hyperthermia elsewhere in the body.

In humans, the perception of thermal comfort or discomfort (i.e. temperature preference) has also been shown to be strongly influenced by the level of core temperature. Indeed, temperature preference can be used as an index of whether a subject is hypo-, normo- or hyper-thermic (Cabanac, 1969; Mower, 1976). If the thermosensitivity of brain structures contributes the major component of the information which gives rise to the perception of thermal comfort or discomfort, then any local change in brain temperature resulting from facial cooling should be made evident by a shift in the temperature preference of the subject. Thus if forced facial fanning of a hyperthermic subject causes local brain cooling, the temperature preference of that subject should shift from that indicative of hyperthermia towards that of a normothermic subject.

METHODS

Eight healthy male subjects in bathing suits were used in a series of experiments done, invariably, between 11.00 and 13.00 h.

Temperature recordings

Body temperatures were recorded with Cu-Const thermocouples from oesophagus (T_{oe}), tympanic membrane (T_{ty}), forehead skin (T_s) and from a skin site just above the angularis oculi vein (T_{ang}). The sensitivity of the measurements was 0·025 °C/mm pen deflection, for all but T_s, the sensitivity of which was 0·25 °C/mm. Total accuracy of measurement was 0·05 °C. The oesophageal thermocouple was passed through the nose down the oesophagus to 0·38 m below the nares. It was assumed to be then lying behind the heart and, so, to be indicating the temperature of central arterial blood. Contact of the tympanic thermocouple with the membrane was evidenced by a dull pain. The auditory canal was then filled with cellulose and taped. The 0·3 mm junction of the thermocouple used for angularis oculi vein temperature recording was bent at a right angle to its wires to obtain the best thermal contact with the vein. This junction, pressing on the skin above angularis oculi vein, was fixed in place by adhesive tape and then well-insulated with a polystyrene block, covering the base of the nose and part of the eyeball. The polystyrene block was taped to the skin, so that no movement of air could occur between the block and the skin. Naked forehead skin temperature was recorded from a thermojunction.

Perceptual rating technique

Throughout the experiment the subject's right hand was exposed to series of thermal stimuli by 30 sec immersion, at 1 min intervals, in a small tank containing water the temperature of which was changed between immersions. The stimulus temperature was recorded from a thermocouple attached to the palm, and the subject was instructed to stir the water continuously with his hand. At the end of each 30 sec stimulus, the subject gave a rating of pleasure or displeasure, according to a scale ranging from +2 (very pleasant), through 0 (indifferent) to −2 (very unpleasant). Previous studies (Cabanac, 1969; Mower, 1976) have shown an inverse relation between preferred stimulus temperature and body core temperature, but in normothermia most of the thermal stimuli are indifferent. In the following, hypo-, normo- and hyperthermia refer to the state of the subjects as judged from their perceptual ratings.

Experimental procedure

To determine the moment when subjects switched from hypothermic to hyperthermic ratings, which was considered to be the point of normothermia, they were immersed in the warm bath when slightly hypothermic. This state was produced by resting the naked subjects at 19–20 °C air temperature for 15–30 min, before they were immersed up to the chin in a well stirred water bath kept at 38·6–38·7 °C. They remained there until the end of the experiment. Their core temperatures increased progressively. When they were clearly hyperthermic, the entire left arm was lifted out and exposed to a 6 m/s wind, produced by a fan, while the head was completely insulated with a plastic bag. After 5–10 min of fanning, the limb was re-immersed, and the uninsulated face was fanned for 30–40 min with the same wind. This fanning changed temperature and relative humidity of air around the face from about 27–28 °C and 70–80 % to 20 °C and 50 %, respectively. Each experiment finished about five min after the fanning ceased.

Analysis of the data

The average upper limit of normothermic body temperature with and without facial fanning was compared for each recorded temperature. The significance of the differences was determined using Student's t test.

RESULTS

Sequence of thermal events in the warm bath

Two different examples of the results are given in Figs. 1 and 2. The subjects were immersed in the warm bath when their perceptual ratings were clearly hypothermic; that is, when cool stimuli were evaluated as unpleasant and warm stimuli as pleasant.

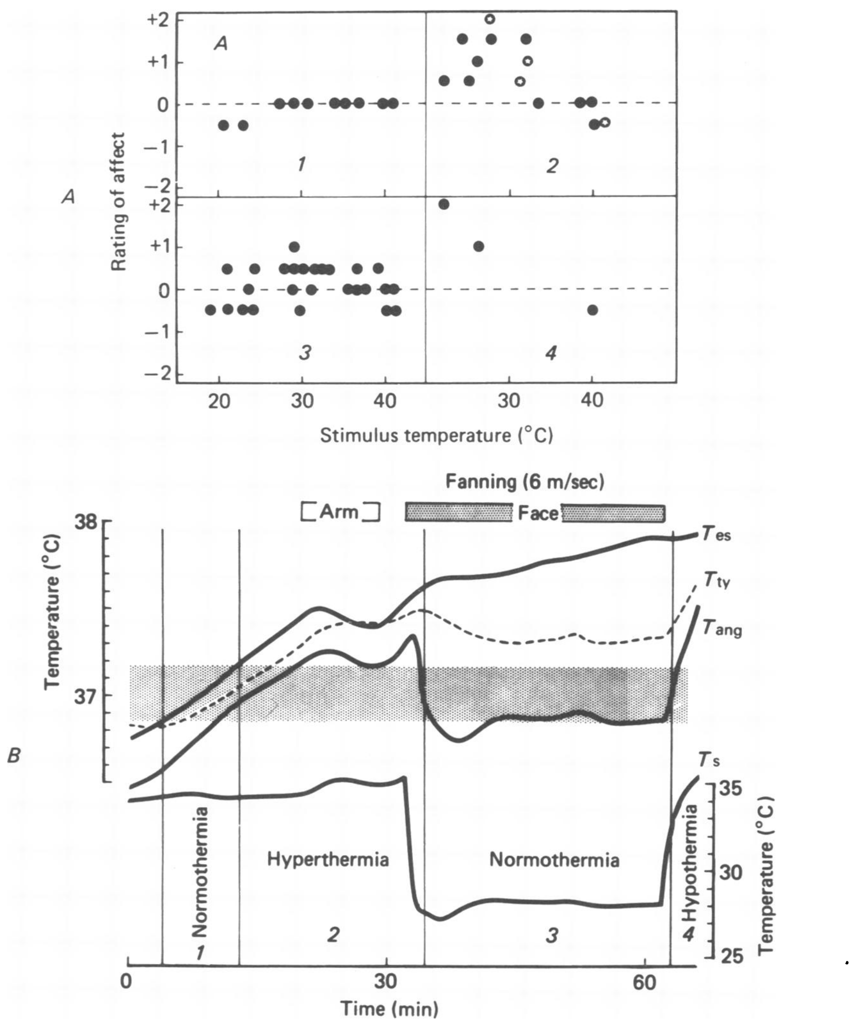

Fig. 1. One example of a typical result.
A, rating (ordinate) of 30 s thermal stimuli (abscissa) imposed on right hand; a star inside a circle means that the opposite arm was being fanned; during period 2, the ratings were of the hyperthermic type whether the arm was being fanned or not. *B*, time course of oesophageal (T_{es}), tympanic (T_{ty}), angularis oculi vein surface (T_{ang}) and forehead temperatures (T_s) in one subject immersed in a warm bath at 38·6 °C; note that T_{es} decreased during arm fanning, which shows its efficacity, but it continued to rise during face fanning. The different populations of perceptual ratings marked by the numbers in *A* were obtained during the time intervals with corresponding numbers indicated between vertical lines in *B*. Horizontal grey band across temperature curves is control normothermic temperature range.

They remained hypothermic for several minutes in the bath, although the subject's skin temperature, which then, of course, equalled the bath temperature, was more than 1·5 °C higher than deep body oesophageal and tympanic temperatures. This

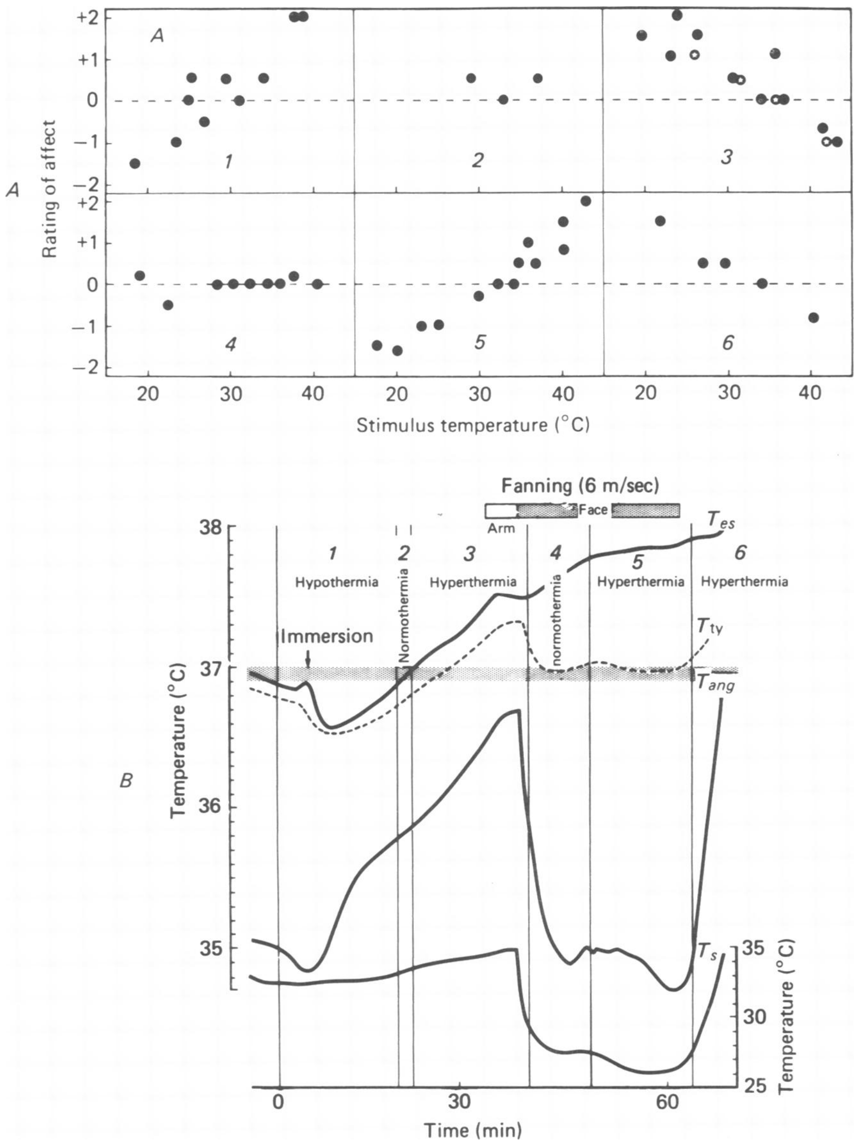

Fig. 2. Same legends as for both *A* and *B* in Fig. 1, but in this example face fanning produced a hypothermic response in the subject who was immersed at the time shown by the arrow. As a result, the ratings produced the six separate patterns shown in *A*; these are separated in *B* by the vertical lines.

temperature gradient produced an increase in body temperatures. As deep body temperature rose, the subjective ratings changed from hypothermic to normothermic, which means that all stimuli became indifferent. Normothermic ratings were given over a range of T_{es} which varied between 0·1 and 0·35 °C. It must be stressed that this normothermic T_{es} was always the same as that at the start of the experiment. Above this range of normothermic T_{es} the ratings became hyperthermic, as evidenced in the examples of Figs. 1 and 2. The cool stimuli were then evaluated as very pleasant, and the warm stimuli as unpleasant. In the hyperthermic phase of the experiment the subjects sweated profusely and sweat flowed down their faces. Throughout the control period of the experiment T_{es} increased scarcely faster than T_{ty}.

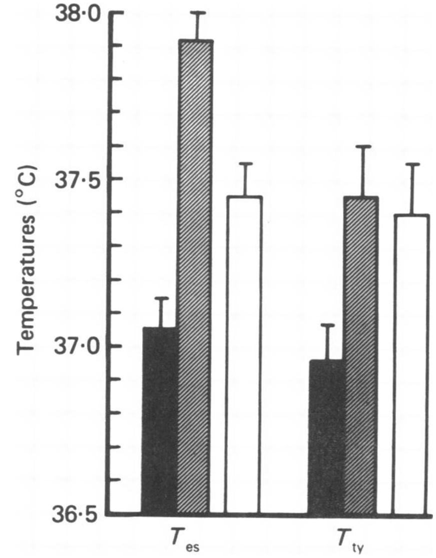

Fig. 3

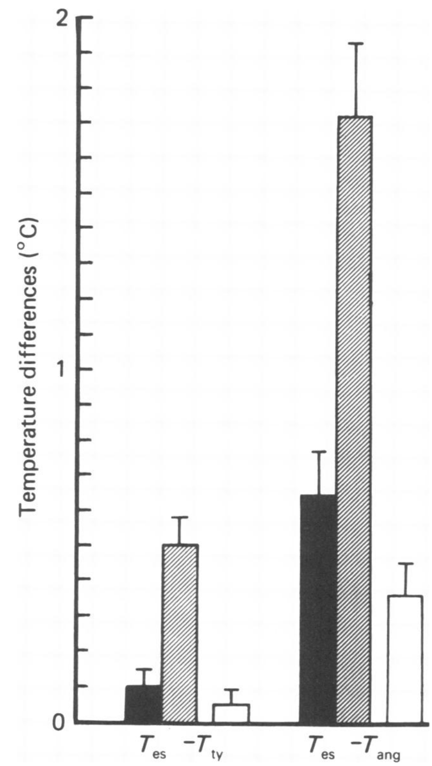

Fig. 4

Fig. 3. Mean upper limits of T_{es} and T_{ty} for normothermic ratings during control period without fanning (black column) and during facial fanning (hatched column). For comparison, mean lower hyperthermic value of both temperatures during control arm fanning is represented by unfilled column. Bars indicate S.E. of the means.

Fig. 4. Mean of the differences between oesophageal and tympanic temperatures ($T_{es} - T_{ty}$), as well as between oesophageal and angularis oculi vein temperatures ($T_{es} - T_{ang}$) during normothermia without fanning (black columns) and during facial fanning (hatched columns). For comparison, lower hyperthermic values of both differences are presented during control arm fanning (unfilled columns). Bars indicate S.E. of the means.

Influence of arm fanning

When the subjects were clearly hyperthermic, the left arm was fanned. This contro fanning resulted in lowering T_{es} while T_{ty} levelled off (Figs. 1 and 2). However, hyperthermic perceptual ratings were totally unchanged by the fanning.

Influence of fanning

The face was fanned either directly after fanning of the arm, as indicated in Fig. 2, or after a lapse of several minutes, during which time body temperature increased again (Fig. 1). This fanning produced an immediate and sharp fall in forehead skin temperature and, afterwards, the angularis oculi vein and tympanic temperatures fell. Two or three minutes later, hyperthermic ratings were replaced by normothermic ones, and even by hypothermic ratings in two subjects, although T_{es} continued to rise. An example of hypothermia accompanying an increase in T_{es} is given in Fig. 2. However, in the majority of subjects the perceptual ratings varied between mildly hypo- and hyperthermic states. This is why widely dispersed ratings, presented in compartment 3 of Fig. 1*A*, are considered normothermic. Facial fanning was so effective that the face was dry.

Stopping of the fan after 1–3 min changed normo- or hypothermic ratings into clearly hyperthermic, and sweat again dripped from the face.

Average results

The average $\pm$ S.E. upper limit of T_{es} for normothermic ratings was $37{\cdot}06 \pm 0{\cdot}09$ °C during the control period without fanning, while this temperature rose to $37{\cdot}91 \pm 0{\cdot}09$ °C during face fanning (Fig. 3). This increase is statistically very significant ($P < 0{\cdot}0005$). Tympanic temperature was also significantly higher ($P < 0{\cdot}05$) during normothermia accompanying facial fanning. On the other hand, the difference between T_{es} and T_{ty} was not significant in control normothermia, but was very significant ($P < 0{\cdot}0025$) in normothermia during facial fanning (Fig. 4). During normothermia accompanying facial fanning, the difference between T_{es} and T_{ang} was $1{\cdot}72 \pm 0{\cdot}22$ °C and was significantly higher ($P < 0{\cdot}01$) than that during control normothermia (Fig. 4).

It must be stressed that T_{es} in normothermia during facial fanning was significantly ($P < 0{\cdot}01$) higher than T_{es} in hyperthermia accompanying control fanning of the arm (Fig. 3).

Forehead skin temperature was $33{\cdot}98 \pm 0{\cdot}24$ °C during control normothermia and dropped to $27{\cdot}96 \pm 0{\cdot}24$ °C during fanning of the face.

DISCUSSION

A previous study (Caputa *et al.* 1978), showed that the direction and speed of the blood flow in the angularis oculi vein depends on deep body temperature. In mild hypothermia blood flowed slowly from the cavernous sinus to the facial venous network. In hyperthermia, however, blood flow was rapid and directed from the facial veins to the cavernous sinus. The present results show that skin temperature near the angularis oculi vein is significantly lowered during facial fanning, although this measurement site was thermally well-insulated.

The selective influence of facial fanning on human brain temperature can be attributed, therefore, to cool venous blood perfusing the cavernous sinus and possibly cooling the blood of the internal carotid artery. Within the sinus, this artery forms a sigmoid siphon which augments the surface at which arterio-venous heat exchange can occur. In ungulates and carnivores such heat exchange has been shown to take place in the cavernous sinus (Baker & Hayward, 1968; Taylor & Lyman, 1972; Baker & Chapman, 1977).

Crawshaw, Nadel, Stolwijk & Stamford (1975) have shown that local cooling of different regions of skin in mildly heat-stressed humans produced cutaneous cold sensation and was immediately followed by a decrease of the rate of sweating, although oesophageal temperature remained unchanged. Therefore they suggested that the inhibition of sweating is effected by neural transmission of the cold signals to the thermoregulatory centres. They presented normalized coefficients of cutaneous cold sensation and sweating inhibition. Both coefficients had the same values during cooling of leg, chest, abdomen and back skin regions, but forehead skin cooling was twice as efficacious on sensation and three times as efficacious in inhibiting sweating. The high efficacity of forehead cooling on sensation could result from a higher density of cold sensors in this skin area (Cabanac, M. & Hugues, J. L. unpublished). However, this inhibitory effect of forehead cooling on sweating could be caused, in part at least, by the selective cooling of the brain. The change in perceptual ratings reported here is certainly unrelated to the stimulation of peripheral cold sensors because this change was absent during left upper arm fanning, although this skin area is more than twice as large as facial skin surface. On the other hand, the cardiovascular changes produced by cooling the face (Leblanc, 1975) may result partly from a direct cooling of the brain.

During face fanning T_{ty} was significantly lower than T_{es}. Nevertheless, it is unlikely that T_{ty} exactly parallels hypothalamic temperature in humans, because the tympanic membrane was significantly warmer during normothermia accompanying face fanning than during control normothermia. Tympanic membrane temperature appears to be modified not only by tympanic arterial blood, but also by jugular venous blood, which passes only a few mm from the membrane within the temporal bone. Therefore this temperature may be recognized only as an undefinable intracranial temperature.

The persistent hypothermic ratings observed in two subjects during face fanning and exemplified in Fig. 2 is a paradoxical phenomenon which we cannot explain. However, fluctuations of perceptual ratings between slightly hypothermic and slightly hyperthermic states were observed in other subjects during face fanning periods, and these appeared to be effected by an 'on-off' type regulation of facial sweating and/or perfusion of cavernous sinus with cool venous blood. This would result in fluctuations of hypothalamic temperature between hypo- and hyperthermic values. The changes in perceptual ratings of hand thermal stimulation during facial fanning indicate that brain temperature, rather than other deep body temperatures, is the major determinant of thermal comfort in humans.

The efficacity of brain cooling by facial fanning is evident when this is compared with arm fanning. The cooling caused by upper limb fanning was sufficient to cause a decrease in general body temperature in subjects while still immersed in warm water. Facial fanning caused the evaporation of the sweat secreted. It is likely that this evaporative heat loss resulted in some cooling of the brain and that the 1 °C increase in T_{es}, which was an open loop increase, is indicative of its magnitude. Change of perceptual ratings from the hyperthermic to normothermic state may be elicited only by a decrease of hypothalamic temperature to, or to below, the level at which normothermic ratings were recorded in the control tests. The magnitude of the selective brain cooling under these conditions is comparable with the 1 °C lowering of brain temperature in the heat-stressed cat (Baker, 1972)

The warm bath and face fanning conditions can be compared with long distance running conditions. In both cases heat is stored inside the body, however the face is ventilated with air of moderate temperature. The wind speed employed in our experiments was nearly the same (6 m/s) as the speeds of champion long distance runners.

It has been shown that at 18·8 °C ambient temperature the deep trunk temperature of a marathon runner may rise to 41·9 °C with no clinical sign of heat illness (Maron, Wagner & Horvath, 1977). It would now seem very likely that under these conditions the brain is kept cooler than other deep body regions, since it would seem impossible for the cerebral integrating function to remain undisturbed if the brain temperature were also elevated by 5 °C. Moreover, it is likely that while selective thermal protection of the large brain in humans prevents cerebral overheating during heavy exercise in cool and moderate thermal conditions, this is negligible during resting in a hot environment. This conclusion is supported by the results of control experiments, in which the upper limit of normothermic ratings in stationary air at 27–28 °C and high humidity did not differ from the normothermic values of oesophageal temperatures at lower ambient temperatures. Therefore, we believe that selective cooling of the human brain, which we have shown under laboratory conditions, really occurs naturally during heavy exercise and can be of comparable magnitude.

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